In the Office action, a number of claimed elements are identified in bold, presumably a notation of the importance of these elements. On page 2 of the Office action, an element noted as (a) is: non-entangled pyvinylpyrrolidone. The Examiner is correct, this is an important element. Yet this element is not found in any of the cited references.

The Background of the Invention section of the present application notes the importance of using a non-entangled separation media. After a brief introduction to capillary electrophoresis, the applicants note that most separation media include an entangled polymer. Such an entangled polymer may be useful for some applications, but it does have drawbacks. First, as noted by the applicants on page 3, such a media requires high pressure introduction of the media into the capillary. Second, the use of entangled polymers is not adaptable to multiple electrokinetic injection of samples.

To eliminate these drawbacks, the applicants in the summary of the invention, require the use of a non-entangled polyvinylprorrolidone for use as a separation media. The applicants note that the "low viscosity of a non-entangled separation media simplifies the filling of microchannels". See Summary, p. 5.

In the detailed description of the invention, the applicants note that high molecular weight polyvinyl-pyrrolidone, having a molecular weight greater than or equal to 1,000,000 have been used as an entangled matrix. On page 7, a method for determining the concentration at which an entanglement threshold is calculated, namely "the point of change of the slope, representing a marked increase in solution viscosity." For 40,000 molecular weight PVP, the entanglement threshold is 11.4% as shown in Fig. 1A and associated text. The application also notes that this threshold will be a lower percentage in the media for higher

molecular weight polymers resulting from their already significant solution viscosity at low concentrations.

The Barry et al. reference does not anticipate the applicants' claim 1 because this reference does not disclose the claimed non-entangled pyvinylpyrrolidone. In section 2.1 of Barry et al., the disclosed separation requires using 1,000,000 molecular weight PVP at a concentration of 14% (w/v). As noted in the applicants' specification, such a separation media would certainly not be considered "non-entangled". The molecular weight is above that which the applicants have stated is allowable. In addition, the threshold cutoff concentration for a lower weight PVP (40,000) is 11.4%. The higher molecular weight PVP used in the cited reference at a higher concentration would be entangled.

The applicants note that one advantage of the use of a non-entangled linear polymer is the low viscosity of the solution allowing low pressure loading into microchannels. However Barry et al. indicate that their media lacks this property of the claimed media. Barry et al. instruct that their PVP media should be introduced into the capillary "by pressure with a syringe" and "replaced by pressure displacement".

Barry et al. does not disclose claimed use of non-entangled pyvinylpyrrolidone. As a result, Barry et al. lacks the advantages of the claimed media, including low pressure loading. This reference does not anticipate the applicants' claim 1 because it does not include one claimed element, a claimed element that the Office action itself has emphasized.

Zhu et al. also fails to disclose the use of non-entangled pyvinylpyrrolidone. The Office action does not cite a single instance of this term in the cited reference, or the properties characteristic of this term. Instead the properties of the polymer used are inconsistent with a non-entangled pyvinylpyrrolidone.

In Zhu et al. column 2 and 3, the authors indicate that the preferred polymer can be up to 2,000,000 molecular weight and up to 200 times the average molecular weight of the sample. As the Office action again indicates in bold, this sample could be a polynucleotide having of 10,000 base pairs. PVP selected using this criteria would not be a non-entangled media, as claimed by the applicants. The applicants have already noted this when discussing this prior art reference at page 2 and 3 of the instant application.

As already noted, one of the defining properties of a non-entangled pyvinylpyrrolidone is the low viscosity, a viscosity below an entanglement threshold. As indicated in Fig. 1A of the applicants' specification, this cutoff is quite low. However the acceptable viscosities disclosed in the Zhu reference at page 5 are significantly higher.

The applicants have already noted in the application that PVP has been used in the past as a separation media component. What has not been disclosed is the use of non-entangled PVP, as defined by the applicants, in the separation media. In the cited reference, the Office action provides only a single use of PVP within the reference, and nothing to indicate within the reference that discloses use of a non-entangled polymer in the media. Instead, the disclosures of this reference indicate that the polymers in the media are entangled. Given this fact, the present claim is not anticipated by this reference as well.

Finally, Madabhushi et al. is cited as anticipating the applicants' claim 1. Again, this rejection should be reconsidered because a method of using a non-entangled pyvinylpyrrolidone is not disclosed. As noted in the applicants' specification, given the size of nucleic acid fragments separated (100-500) entanglement of the linear polymers is a prerequisite for the separation described in Madabhushi to work. In column 8 of Madabhushi, the claimed method is noted as having a charge carrying component, a

sieving component, and a surface interaction component. PVP is used as the surface interaction component. Given that this reference actually specifies the use of a sieving component, the use of a non-entangled polymer would be unimportant an is simply not disclosed. Given that none of the references disclosed at least one of the claimed elements, the rejection of claim 1 as anticipated should be reconsidered and withdrawn.

A second of the applicants' claimed elements (also highlighted in the Office action) is the separation of fragments between 0 and 100 bases. However, Barry et al. is limited to the separation of four-mer and five-mer modified oligonucleotides. Given that a reference can only anticipate if every element is found within the cited reference, this is a second independent reason to withdraw the rejection based on Barry et. al.

Dependent claims

The law for determining whether a claim is anticipated requires that each and every claim element must be found in the cited reference. While the Office action addresses claim 1, no statement was made about claims 2-17. Given that no prima facie case for rejection of these claims was made, they should all be found allowable.

A number of the elements in the dependent claims simply could never be found in the cited references because the claimed method is directed to a wholly different purpose than the cited references. For example, claim 4 is directed to a specific method of loading the capillary using gas pressure loading at a relatively low pressure. Not only do the cited references not disclose this claimed step, it would simply not be possible to fill a capillary with high viscosity entangled media using such low pressure. This fact not only indicates the novelty of claim 4, it also reinforces the

novelty of claim 1. It is the use of a low viscosity non-entangled media of claim 1 that makes claim 4 possible.

Applicants' claim 8 is directed to a method in which the injection and separation steps are repeated. In such a claimed method a first sample is injected, current is introduced and the sample migrates through a length of the microchannel, a second sample is introduced, the then both injected samples migrate as current is applied. Both samples may be subsequently sequentially detected. Again, not only is this step not found in the cited references, the cited references disclose only entangled separation media in which such a method would degrade the media and the separation, as noted in the applicants' specification. Again, not only is claim 8 not anticipated, but this shows a reason why claim 1 is not anticipated as well.

Given that nothing has been cited as anticipating any of the applicants' dependent claims, all of claims 2-18 should be found to be allowable.

Conclusion

In light of the foregoing remarks, the present rejection should be reconsidered. A notice of allowance is earnestly solicited. If the Examiner has any questions in relation to this matter, please contact the undersigned attorney at (408) 297-9733 between 9 AM and 5PM Pacific Time.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Signed: Merle P. Garcia
Typed Name: Merle P. Garcia

Date: June 16, 2004